EPITHELIOMA OF HAND—A STUDY IN DIFFERENTIAL DIAGNOSIS BETWEEN EPITHELIOMA AND ENDOTHELIOMA*

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In October, 1922, a rancher, 61 years old, applied for treatment, complaining of ulcers on his right hand and arm. He said that six years ago he ran a splinter into the back of his right hand and that soon after this a lump appeared at the site of the injury. This lump persisted and broke down, and discharged pus intermittently. More than five years later, about four months ago, after pulling on a rope, red streaks appeared on both arms. Those on the right arm remained, the others soon disappeared. The right hand swelled, and a swelling appeared in the right axilla. The latter was opened and a large amount of foul semi-fluid necrotic material was removed.

One week later the lump on the hand was excised. This was examined at a laboratory and the patient informed that it was not cancer. Ten days later a lump appeared on the anterior aspect of the wrist, and following this other lumps appeared, extending successively up the arm as far as the axilla. Most of these lumps eventually broke down and discharged.

When the patient came to me he presented a most remarkable picture. On the back of the right hand was an ulcerated nodule 2½ x 4½ cm., undoubtedly a recurrent lesion at the site of the original injury. On either side of this were scars, the result of the old excision. Proceeding now mesially around the wrist and extending directly upward on the flexor surface of the arm was a striking series of similar nodules. These were of different ages and sizes, ranging from ¾ to 3½ cm. in diameter. All but one or two were quite definitely ulcerated. When close together the nodules tended to coalesce into a single large area with raised irregular borders and ragged excavated center. Two such areas were present at the wrist and in the axilla, measuring 7½x14½ cm. and 4½x9½ cm., respectively. Where discrete the nodules appeared typically as bluntly acuminate swellings marked by thick rounded borders and sharp crater-like centers. At times two neighboring lesions were joined by a narrow subcutaneous passage. A distinctive clinical feature observed was the outpouring of an abundant pale watery turbid fluid from all of the open lesions. Associated with the above was a marked diffuse swelling of both the hand and arm to about twice normal size.

Such was the gross picture, and the first point to be settled was that of diagnosis. With the history as outlined above, some form of infection was quite naturally suspected. Cultures were made from the lesions; the discharge examined for coccidioidiosis, actinomycosis, sporotrichosis, and oidiomycosis. The ulcer borders were biopsied and frozen sections prepared. The bacteriological studies were negative. Smears of the discharge from several of the lesions were also negative. The frozen sections, however, yielded a clue, for they showed a form of new-growth. This from the first appeared unusual. That it was malignant was obvious, but just what type the cells might be could not be determined so readily. Owing, however, to the presence of certain marked characteristics to be described later the diag-

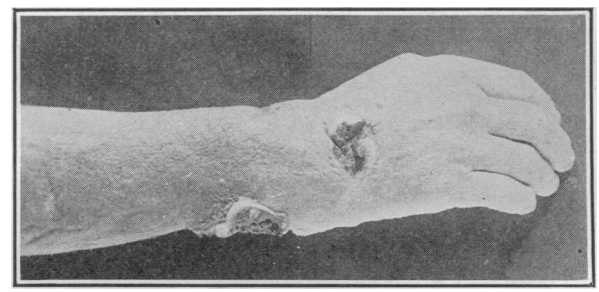

Fig. 1—Showing the recurrent ulcerated nodule on the back of the hand at the site of the original lesion.

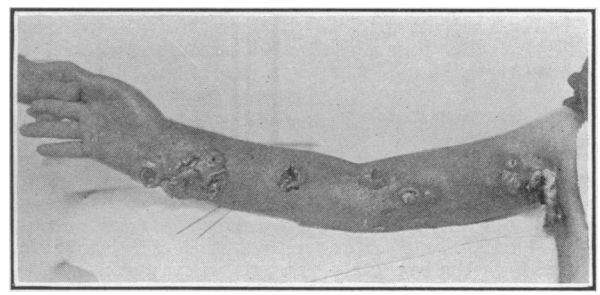

Fig. 2—Showing the general distribution of the lesions up the front of the arm, with the large coalescent areas at the wrist and axilla.

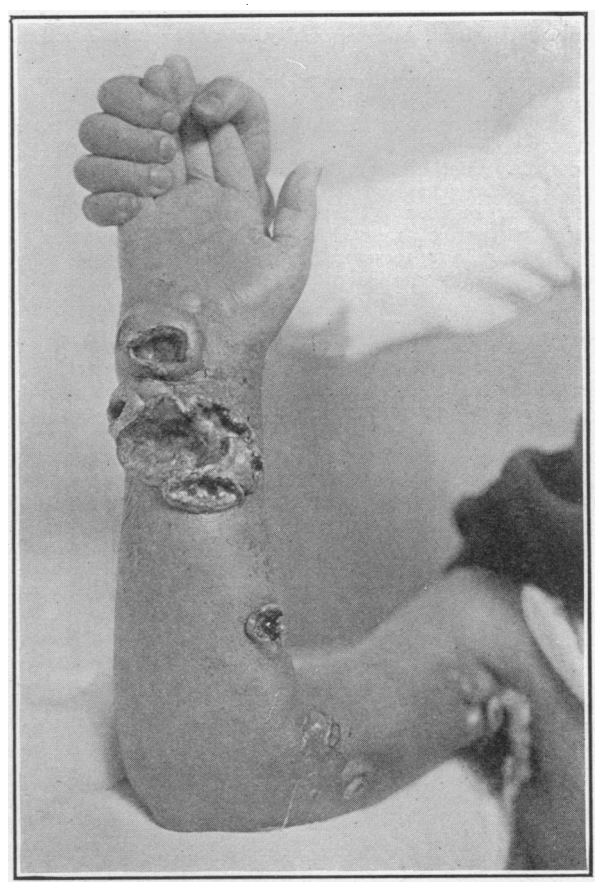

Fig. 3—Showing both discrete and conglomerate lesions with the gross characteristics of each; note the crater-like centers.

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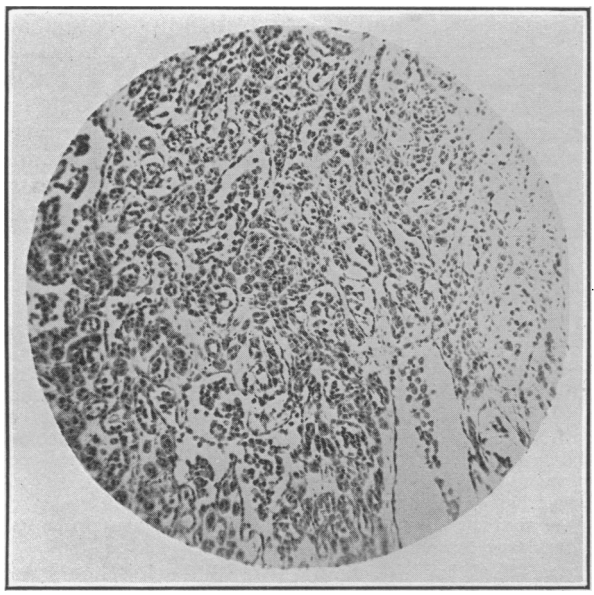

Fig 4—Showing the peculiar cell-lined spaces, also the arrangement of tumor cells between the spaces.

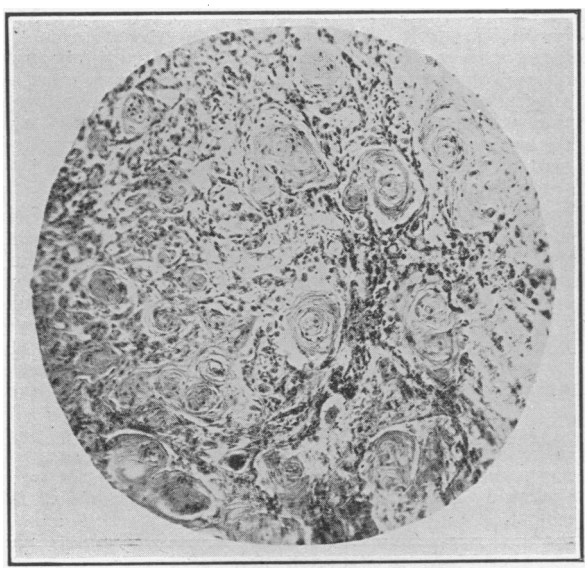

Fig. 5—Showing the cell whorls.

nosis of endothelioma was strongly suggested, and such a diagnosis was tentatively rendered.

The patient was in fair general condition, the tumor apparently limited to the arm, and the chance for cure at least possible. A shoulder-girdle amputation was therefore performed. The man made a good recovery, suffered no complications, and left the hospital two months later in excellent physical condition.

Further studies were made of the lesions. Grossly the tissue was firm and semi-elastic, and on section homogeneous, gray-white and succulent.

Microscopically the sections showed an extensive tumor invasion. This involved primarily the corium and adjacent subcutaneous tissue. From thence it extended upward to invade the overlying epithelium. The general appearance of the growth presented two noteworthy features. The first was the presence of numerous clear-cut spaces, easily seen, and of various shapes and sizes. Some were large and round or oval, others were mere branching crevices. All were lined by a continuous layer of tumor cells. Of these some were large and plump, others bore a triangular appearance with the point projecting into the lumen; while yet others were flatter in outline, though still showing a bulging free surface. Not infrequently all three varieties were intermingled together in the same space, irregularly alternating. The lumina themselves were varied; some were entirely empty, others were filled with the tumor cells, and still others were only partly filled. In the last the cells lay either entirely free or piled up at one end as though proliferated from the adjacent underlying tumor cells. Nothing suggestive of an endothelial lining could be made out external to the tumor cells. In none of the spaces was blood seen.

Between the spaces were other tumor cells vari-

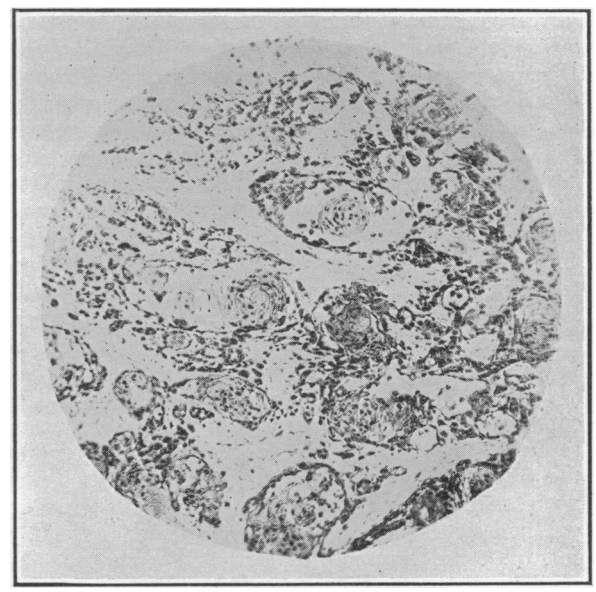

Fig. 6—Another view of the whorls, showing them inside as well as outside the spaces.

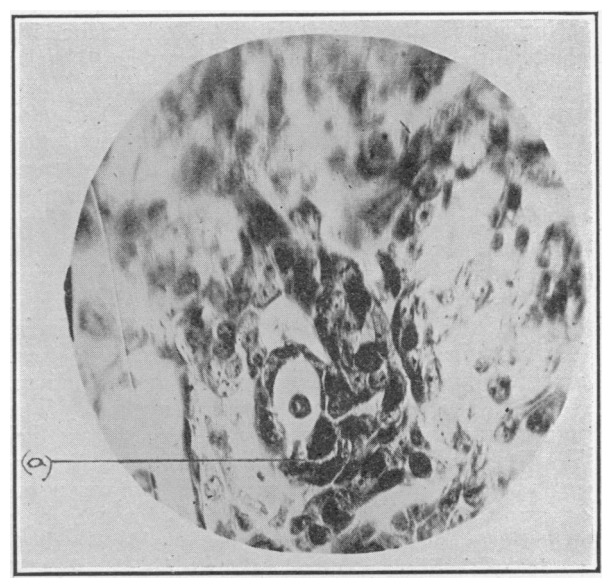

Fig. 7—A high power view of the tumor cells, showing the "prickles" (a) and the nucleoli.

ously arranged, sometimes in long branching columns, again in small rounded or oval areas, and still again in larger sheet-like masses. Some of the columns showed fissures, suggesting lumen formation.

The second striking characteristic was the presence of large numbers of sharply outlined rounded bodies resembling epithelial "pearls." These were composed of tumor cells compactly arranged in concentric whorls, and were irregularly distributed throughout the growth, occurring about equally within and outside the spaces.

The tumor cells themselves were fairly uniform in size with an abundant pale staining cytoplasm, finely reticulated and sharply outlined, and with nuclei that were large and vesicular and supplied with only a small amount of chromatin. Mitotic figures were numerous.

Up to this point the description might very well apply to the tentative diagnosis, endothelioma, due to the histology of the cells, the formation of numerous spaces, and the presence of the pearl-like whorls. If also we were to add the abundant watery discharge described we might be justified in going even further and using the term lymphangio-endothelioma. In this, however, it seems not impossible that we may have been somewhat influenced by recalling in Mallory's Principles of Pathologic Histology a cavernous haemangio-endothelioma with a lesion distribution very similar to that just described. And then more recently Busman described a case that both grossly and microscopically very closely resembles our own.

Despite such confirmatory evidences, however, we were not yet definitely assured as to the correctness of our diagnosis. Recourse, therefore, was had to certain differential stains and to further attention to detail. By these means we were able to determine the three following additional points: First, it was noted that practically all of the tumor cells possessed one and sometimes two or three distinct nucleoli, a feature more common to epithelial than to endothelial cells; secondly, some of the cells were found to have a quite definite border of very fine protoplasmic projections or "prickles," demonstrated by the Mallory acid phosphotungstic haematoxylin stain; and finally, in certain of the cells composing the whorls there were seen distinct kerato-hyalin granules, shown best by the Gram's stain. These last two points were particularly important, for prickle cells and keratohyalin granules are not found in endothelial structures (Ewing). It thus became necessary to reconsider our previous diagnosis and to transfer the tumor from the group of endothelioma to that of epithelioma.

Concerning the method of spread, the following may be stated: The extension was relatively slow. The nodules were all external to the deep fascia, invading the corium and subcutaneous tissue first, and subsequently ulcerating through the epithelium. The axillary nodes were definitely involved. The tumor was growing within numerous thin-walled bloodless spaces in which endothelium had apparently been replaced by tumor cells. There was never at any time any hemorrhage from even the most extensively ulcerated of the lesions. All of which tended to indicate a spread of the tumor by way of the lymphatics.

The later history of the patient can be briefly disposed of. From the two or three communications irregularly received we learned that shortly after his discharge from the hospital there developed at the site of the wound first one nodule, then another; that the man continued to lose ground slowly, but steadily; and that at the last writing (May, 1923) he was in the hands of a sure-cure cancer doctor in Oklahoma, undergoing a plaster-poultice method of treatment.

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DISCUSSION

Howard Morrow, M. D. (380 Post Street, San Francisco)—In my experience the condition was a clinical entity. The great number of ulcers limited to the hand, forearm and arm, the profuse weeping from the individual ulcers, the lack of dense infiltration in the borders of the ulcers, and the absence of systemic growths, were conditions which made the clinical picture unique. It was difficult further to eliminate sporotrichosis clinically. The differentiation of endothelioma from an atypical carcinoma must remain in the hands of the pathologist.

G. Y. Rusk, M. D. (U. C. Medical School, San Francisco)—Through the courtesy of Dr. Morrow I had an opportunity to see the case clinically as well as to follow Dr. Perkins' careful and thorough study of the growth. The distribution along the superficial lymphatics, with the numerous outcroppings in the form of weeping ulcers, strongly suggested to my mind an endothelioma. The early frozen sections were inadequate to make a differential diagnosis. The direction which the investigation took, the findings, and the reasons for the ultimate diagnosis are clearly presented in Dr. Perkins' paper.

W. A. Perkins, M. D.—The laboratory report on the tissue from the original nodule removed four months ago was "not cancer." We regret that this work was done so far away (in Arizona), precluding further investigation of that point. Had the patient remained longer in the hospital it is possible that suitable treatment of the local recurrences of the growth might have resulted in a complete eradication of the tumor. One or two x-ray treatments had been given before discharge of the patient, but these proved insufficient.

I wish to thank Doctor Morrow for the privilege of reporting this case, and Doctor Rusk for the many suggestions and valuable assistance which he gave in the study of the material and the preparation of the report.

A Non-Elastic Faith—"The Christian Science Monitor expresses hot indignation at measures that have checked foot and mouth disease in California," says Colorado Medicine.

"'Los Angeles,' it says, 'and a considerable portion of the country thereabouts, have been subjected for the last few weeks to an extraordinary manifestation of the results of hysteria caused by medical superstition and medical domination. Because of an alleged epidemic of what is called foot-and-mouth disease among the cattle in adjacent regions, the veterinarians and the health boards of that section have been assuming powers hitherto unknown to the most notorious autocrats of history.'

"The Monitor should be more tolerant. It cannot expect animals with foot and mouth disease to read Science and Health, and it can scarcely hope to convince them that there is no such thing as disease. Why not, then, fashion the faith a little, and persuade Christian Scientists that there is no such thing as quarantine?"

"Efficient government is not the result of a shifting series of political expedients, nor can free institutions be permanently maintained without rigid adherence to certain basic truths."—J. H. Beal, The Force Behind the Law.